

United States Patent and Trademark Office

UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address COMMISSUNER OF PATENTS AND TRADEMARKS Washington D C 20231 www.o-po.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	A FTORNEY DOCKET NO.	CONFIRMATION NO
09/770,601	01/26/2001	Myra A. Lipes	10276-015002	6880
26161	7590 01/14/2003			
FISH & RICHARDSON PC			EXAMINER	
225 FRANKI BOSTON, M			FALK, ANNE MARIE	
			ART UNIT	PAPER NUMBER
			1632 DATE MAILED: 01,14 2003	13

Please find below and/or attached an Office communication concerning this application or proceeding.

		rile			
	Application No.	Applicant(s)			
	09/770,601	LIPES ET AL.			
Office Action Summary	Examiner	Art Unit			
TI. MAU INO DATE Africa	Anne-Marie Falk, Ph.D.	1632			
The MAILING DATE of this communication app Period for Reply	ears on the cover sheet with the c	orrespondenc address			
A SHORTENED STATUTORY PERIOD FOR REPLY THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply - If NO period for reply is specified above, the maximum statutory period w - Failure to reply within the set or extended period for reply will, by statute, - Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b). Status	16(a). In no event, however, may a reply be time within the statutory minimum of thirty (30) days ill apply and will expire SIX (6) MONTHS from cause the application to become ABANDONE	nely filed s will be considered timely. the mailing date of this communication. O (35 U.S.C. § 133).			
1) Responsive to communication(s) filed on 10 S	September 2002 .				
2a) ☐ This action is FINAL . 2b) ☑ Thi	s action is non-final.				
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213. Disposition of Claims					
4) Claim(s) 26-38 is/are pending in the applicatio	n.				
4a) Of the above claim(s) 32-38 is/are withdraw	n from consideration.				
5) Claim(s) is/are allowed.					
6) Claim(s) 26-31 is/are rejected.					
7) Claim(s) is/are objected to.					
8) Claim(s) are subject to restriction and/or	election requirement.				
Application Papers					
9) The specification is objected to by the Examiner.					
10) The drawing(s) filed on is/are: a) □ accepted or b) □ objected to by the Examiner.					
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).					
11) The proposed drawing correction filed on is: a) approved b) disapproved by the Examiner.					
If approved, corrected drawings are required in reply to this Office action. 12) The oath or declaration is objected to by the Examiner.					
Priority under 35 U.S.C. §§ 119 and 120	2(1)11(01)				
13) Acknowledgment is made of a claim for foreign	priority under 35 H.S.C. & 119/a	\-(d) or (f)			
a) All b) Some * c) None of:	phoney under 65 5.5.5. 3 115(a))-(d) 01 (i).			
1. Certified copies of the priority documents	have been received				
2. Certified copies of the priority documents		on No			
Copies of the certified copies of the prior application from the International Bur See the attached detailed Office action for a list of the certified copies of the prior application from the International Bur	ity documents have been receive eau (PCT Rule 17.2(a)).	d in this National Stage			
14)⊠ Acknowledgment is made of a claim for domestic	•				
a) ☐ The translation of the foreign language products Acknowledgment is made of a claim for domestic	visional application has been rec	eived.			
Attachment(s)	. ,				
Notice of References Cited (PTO-892) Notice of Draftsperson's Patent Drawing Review (PTO-948) Information Disclosure Statement(s) (PTO-1449) Paper No(s)	5) 🔲 Notice of Informal P	(PTO-413) Paper No(s) Patent Application (PTO-152)			
Patent and Trademark Office					

Art Unit: 1632

DETAILED ACTION

The response filed September 10, 2002 (Paper No. 11) has been entered. Applicants' election without traverse of Group I, Claims 26-31 in Paper No. 11 is acknowledged. The elected invention is drawn to a method of producing a protein in a subject *in vivo* by introducing into the subject an immunologically privileged cell which expresses the protein.

The amendment filed November 4, 2002 (Paper No. 12) has been entered.

Claims 26-38 are pending in the instant application.

Claims 32-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. The election was made without traverse in Paper No. 11.

Accordingly, Claims 26-31 are examined herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 26-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a method of producing a protein in a subject *in vivo* by introducing into the subject an immunologically privileged cell which expresses the protein.

The specification fails to provide an enabling disclosure for using the claimed method in therapeutic transplantation. However, the specification discloses that the only use for the claimed method

Application/Control Number: 09/770,601

Art Unit: 1632

is to provide a therapeutic effect in a subject. Thus, the specification must be enabling for therapeutic transplantation, as this is the sole asserted utility for the claimed method. The specification does not offer specific guidance as to how the claimed method could be used therapeutically for any disorder. No working examples demonstrate a therapeutic effect upon transplantation of the cells recited in the claims. The specification fails to provide specific guidance relating to the amount of cells to inject, the site of injection, and extent of cellular persistence, required to provide any therapeutic benefit for any disorder.

The court has recognized that physiological activity is unpredictable. *In re Fisher*, 166 USPQ 18 (CCPA 1970). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. *In re Fisher*, 166 USPQ 18 (CCPA 1970).

The claimed methods encompass *ex vivo* gene therapy. However, gene therapy is not routinely successful. Therefore, the disclosure must enable the full scope of the claims with specific guidance. However, the specification fails to teach any method for transferring any gene into a target cell and expressing that gene at a level sufficient to produce a therapeutic effect in a diseased immunocompetent animal. The specification does not provide sufficient guidance as to the level of gene expression required, the number of transduced cells needed, the route and time course of administration, the site of administration, when, where, or for how long the exogenous gene should be expressed, the frequency of administration of the genetically-modified cells (i.e., the gene therapy vector) required, or the intended target tissue, for treatment of any pathological condition in an immunocompetent animal. The specification also lacks any working examples showing that the claimed cells, once delivered to an appropriate site, would express the exogenous gene at a level sufficient to provide adequate product to effect the desired therapy in an immunocompetent animal. At the time the application was filed, the art of administering any type of genetic expression vector to an individual so as to provide a tangible therapeutic benefit was poorly developed and unpredictable. The NIH ad hoc committee to assess the

Application/Control Number: 09/770,601

Art Unit: 1632

current status and promise of gene therapy reported in December 1995 that "clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol, despite anecdotal claims...," and that "significant problems remain in all basic aspects of gene therapy" (Orkin and Motulsky, p. 1). In a review article published in Scientific American in June 1997, Theodore Friedmann discusses the technical barriers which have so far prevented successful gene therapy, and states "So far, however, no approach has definitively improved the health of a single one of the more than 2,000 patients who have enrolled in gene therapy trials worldwide" (p. 96). In a review article published in Nature in September 1997, Inder Verma states "Although more than 200 clinical trials are currently underway worldwide, with hundreds of patients enrolled, there is still no single outcome that we can point to as a success story" (p. 239). The instant specification does not adequately teach one skilled in the art how to use the claimed compositions for ex vivo gene therapy. Thus, absent any showing that the claimed methods can be used in gene therapy applications to produce the intended therapeutic effect in an immunocompetent animal, such as a human, claims directed to genetically modified cells are not enabled by the disclosure.

Page 4

In view of the quantity of experimentation necessary to determine appropriate parameters for using the claimed methods of transplantation to achieve a therapeutic outcome, and given the lack of applicable working examples directed to the rapeutic transplantation, the limited guidance in the specification with regard to transplantation protocols and their applicability to pathologic conditions, the broad scope of the claims with regard to the wide variety of genetically modified cells that could be used, and further given the unpredictability in the art of therapeutic transplantation, undue experimentation would have been required for one skilled in the art to make and use the claimed methods.

Conclusion

No claims are allowable.

Application/Control Number: 09/770,601

Art Unit: 1632

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, William Phillips, whose telephone number is (703) 305-3482.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk, PH.D
PRIMARY EXAMINER

Page 5